



**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
-----------------	-------------	----------------------	---------------------

09/269,321 09/13/99 KAELIN JR. W 46793

RONALD I EISENSTEIN
NIXON PEABODY
101 FEDERAL STREET
BOSTON MA 02110

HM12/0323

EXAMINER

SANDALS, W

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 03/23/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/269,321

Applicant(s)

Fine et al.

Examiner

WILLIAM SANDALS

Group Art Unit
1636

☒ Responsive to communication(s) filed on Jan 6, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 15-26 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 15-26 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1636

DETAILED ACTION

Inventorship

1. In view of the papers filed January 11, 2000, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by adding inventors Donald W. Kufe, Yoshino Manume and Rakesh Datta.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

3. The use of the trademarks CYTOVENE, MINOTOME, TWEEN and VECTASTAIN have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Art Unit: 1636

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

4. Claims 15 and 18 are objected to because in line 1 the word "cassettes" is plural and should be singular.
5. Claim 25 is objected to because in line 6 "operable" should be **"operably"**.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 15-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cells in-vitro, does not reasonably provide enablement for cells in an animal, in-vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification contains references to methods of gene therapy, and the claims are drawn to a method of selectively targeting a malignant cell. While applicants have shown

Art Unit: 1636

examples of targeting a malignant cell *in vitro*, they have not demonstrated any method of targeting a malignant cell *in vivo*. In order to do so, undue experimentation is required. Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors. Many of these factors have been summarized in *In re Wands*, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).

The Wands factors as they apply to the instant claimed invention are as follows:

- a- The quantity of experimentation necessary to reduce the instant claimed invention to practice would involve developing a gene therapy method.
- b- Examples have been provided which show the introduction of a vector into normal rat brain tissue, and some *in vitro* examples of the method. However, no examples of gene therapy have been demonstrated, and the application provides only limited, prophetic teachings on the method of targeting a malignant cell *in vivo*.
- d- The nature of the invention is complex. Gene therapy is a new and developing art as recited in Marshall in the section titled "The trouble with vectors", and at page 1054, column 3, and at page 1055, column 3. The problems of gene delivery, gene targeting to reach the intended host cell, and then to reach the intracellular target are not yet solved, as taught in Verma et al. (see especially page 239, column 3, the box titled "What makes an ideal vector?" and page 242).
- d- The prior art taught by Orkin et al. (see especially the section on "Gene transfer and expression" and "Gene therapy in man status of the field") described many problems in the developing field of gene therapy. Recited problems include: lack of efficacy, adverse short term

Art Unit: 1636

effects and limited clinical experience, the inability to extrapolate experimental results and unreliability of animal models. Problems with the vector include: host immune response to the vector and the expressed product, difficulty of targeting the vector to the desired site, transient expression of the gene of interest and low efficiency of delivery of the vector to the targeted site.

f- The state of the art as taught by Verma et al., which states “the problems - such as the lack of efficient delivery systems, lack of sustained expression, and host immune reactions - remain formidable problems” and Anderson, W. F. (see page 25, top of column 1), which states “[e]xcept for anecdotal reports of individual patients being helped, there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human disease”.

g- Therefore, given the analysis above, it must be considered that the skilled artisan would have needed to have practiced considerable non-routine, trial and error experimentation to enable the full scope of the claims.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 15-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1636

10. Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting an essential step, such omission does not set forth the method in clear and unambiguous terms. See MPEP § 2172.01. The omitted step is a correlation, or recapitulation step at the end of the claim which restates the preamble.

11. Claims 19 and 25 are rejected as being unclear since the term “negative potentiator” (and “positive potentiator”) is not an art recognized term and “negative potentiator” (and “positive potentiator”) is not defined in the claims or specification.

12. Claim 20 is rejected as being unclear because the term “dominant negative mutant” is not defined in the claims or specification.

13. Claim 23 is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. In the present instance, claim 23 depends from claim 20 which recites that the gene of interest is a negative potentiator. Claim 23 further depends from claim 21 which recites the negative potentiator is a suicide gene, and claim 22 depends from claim 21 where claim 22 recites that the suicide gene is a thymidine kinase gene. Claim 23 depends from claim 22 wherein the negative potentiator gene is a suicide gene which is a thymidine kinase gene, and then goes on to claim that this gene is a cytotoxin which also contains at least domain III or pseudomonas exotoxin A. It is not explained how the thymidine kinase gene will contain a pseudomonas exotoxin A domain III. Therefore the claim is undefined and unclear. Changing the dependency of the claim to one of claims 19 or 20 would cure this deficiency.

Art Unit: 1636

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

15. Claims 15, 25 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No. 5,885,833.

US Pat No. 5,885,833 taught (see especially the abstract, the summary, and columns 5-8 and 11-21) the transfecting of a glioma cell with a viral vector (which may be an adeno-associated viral vector) or a plasmid which comprised an E2F responsive DHFR, Pol alpha, BMyb or cMyc promoter or E2F enhancer element which controls expression of an activator sequence, which may be a TK gene or a cytotoxin (see column 12).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1636

17. Claims 15-23 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raj et al. or Xiao et al. or US Pat No. 5,885,833 in view of WO 94/18992 and US Pat No. 5,529,774.

Raj et al. taught (see especially the abstract, the introduction, page 1281, column 2 and the figures) the transfecting of a glioma cell with a plasmid which comprised an E2F responsive

Xiao et al. taught (see especially the abstract and page 697, column 1 and the figures) the transfecting of a glioma cell with a plasmid which comprised an E2F responsive promoter.

US Pat No. 5,885,833 taught the invention as described above.

Raj et al. or Xiao et al. or US Pat No. 5,885,833 did not teach that the viral vector was an adenovirus vector or a herpes virus vector.

WO 94/18992 taught (see especially the abstract and page 27) the advantageous use of an adenoviral vector to deliver a thymidine kinase gene to tumor cells, which may be glioma cells.

US Pat No. 5,529,774 taught the advantageous use of retroviral vectors to deliver a thymidine kinase gene to glioma cells.

Since the claims also read on *in vitro* applications of the method, it would have been obvious to one of ordinary skill in the art at the time of filing of the instant application to combine the method of transfecting of a glioma cell with a viral vector or plasmid which comprised an E2F responsive DHFR, Pol alpha, or cMyc promoter or E2F enhancer element as taught by each of Raj et al. or Xiao et al. or US Pat No. 5,885,833 with the adenoviral or retroviral vectors of WO 94/18992 and US Pat No. 5,529,774 because WO 94/18992 and US Pat

Art Unit: 1636

No. 5,529,774 taught the advantageous and well known use of viral vectors to transfect a target cell, where the viral vector comprised a thymidine kinase cytotoxic gene.

One of ordinary skill in the art would have been motivated at the time of filing of the instant application to combine the method of transfecting of a glioma cell with a viral vector or plasmid which comprised an E2F responsive DHFR, Pol alpha, or cMyc promoter or E2F enhancer element as taught by each of Raj et al. or Xiao et al. or US Pat No. 5,885,833 with the adenoviral or retroviral vectors of WO 94/18992 and US Pat No. 5,529,774 because US Pat No. 5,885,833 taught the advantageous use of viral vectors to practice the method, and WO 94/18992 and US Pat No. 5,529,774 taught the advantageous and well known use of viral vectors to transfect a target cell, where the viral vector comprised a thymidine kinase cytotoxic gene. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Raj et al. or Xiao et al. or US Pat No. 5,885,833 with WO 94/18992 and US Pat No. 5,529,774.

Conclusion

18. Certain papers related to this application are *welcomed* to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Art Unit: 1636

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

William Sandals, Ph.D.
Examiner
March 20, 2000


ROBERT A. SCHWARTZMAN
PATENT EXAMINER

09/269321
10/49

Search Results - Record(s) 1 through 9 of 9 returned.

1. Document ID: US 5972643 A
Entry 1 of 9

File: USPT

Oct 26, 1999

DOCUMENT-IDENTIFIER: US 5972643 A
TITLE: Isolated polynucleotide molecules encoding CTCF, a CCCTC-binding factor

BSPR:

Despite recent progress in defining the mechanism of myc action on "down stream" events, less

progress has been made in defining the proteins regulating the expression of c-myc itself. Both transcriptional and post-transcriptional mechanisms appear to play a role in regulation of c-myc

gene expression (Cole, Annu. Rev. Genet. 20:361-384 (1986), Spencer et al., Cancer Res. 56:1-48

(1991), and Marcu et al., Annual Rev. Biochem. 61:809-860 (1992), each of which is incorporated

herein by reference). Maintenance of the level of the c-myc mRNA is achieved by regulation of

both transcriptional initiation and elongation. Both initiation, and elongation of the c-myc

mRNA, depend upon promoter elements which interact specifically with particular nuclear factors

(Spencer, Oncogene 5:777-785 (1990) and Spencer et al., Cancer Res. 56:1-48 (1991), each of which

is incorporated herein by reference). A general map of mouse and human c-myc transcription

elements has been suggested and nuclear factors which bind to these elements have been reported.

In certain cases novel cDNA's encoding such factors have been isolated and sequenced including:

ZF87 (also called MAZ), a proline-rich six Zn-finger protein binding to ME1a1/ME1a2 elements

within P2 promoter of the murine c-myc gene (Pyrce et al., Biochem. 31:4102-4110 (1992) and

Bossone et al., Proc. Natl. Acad. Sci. USA, 89:7452-7456 (1992), each of which is incorporated

herein by reference); a 37-kDa protein, MBP-1, which appears to be a negative regulator of the

human c-myc promoter (Ray et al., Mol. Cell. Biol. 11:2154-2161 (1991), incorporated herein by

reference); and nuclease sensitive element protein-1 (NSEP-1) which binds to a region necessary

for efficient P2 initiation (Kolluri and Kinniburgh, Nucl. Acids Res. 17:4771 (1991),

incorporated herein by reference). In addition, an Rb binding protein E2F which recognizes an

E1A-transactivation site in the human c-myc promoter (Thalmeier et al., Genes Dev. 3:527-536

(1989), incorporated herein by reference) has also been cloned (Helin et al., Cell 70:337-350

(1992), incorporated herein by reference).

2. Document ID: US 5965368 A
Entry 2 of 9

File: USPT

Oct 12, 1999

DOCUMENT-IDENTIFIER: US 5965368 A
TITLE: Reverse two-hybrid systems

DEPR:

To determine whether the newly isolated alleles exhibit similar phenotypes, protein binding

assays can be used. For example, each E2F allele can be tested in an in

vitro binding assay that

involves amplifying, in a PCR reaction, the sequences encoding the various E2F alleles. An

example of an appropriate 5' primer is one which has 25 nucleotides corresponding to the phage T7

RNA polymerase promoter sequence and 20 nucleotides that correspond to the activation domain near

the junction of the activation domain and amino acid 159 of E2F1 (i.e., the first E2F1 amino

acid). A suitable 3' primer is one which corresponds to the 3' end of the E2F1 sequence. The PCR

products from amplification of this sequence can be used in an in vitro transcription/translation

system to generate the corresponding proteins. The mutant proteins can be bound to hybrid

proteins having wild-type DP1 bound to glutathione-S-transferase.

Interacting pairs of proteins

can be purified with glutathione agarose beads, released from the beads, and analyzed by

SDS-polyacrylamide gel electrophoresis.

3. Document ID: US 5955280 A
Entry 3 of 9

File: USPT

Sep 21, 1999

DOCUMENT-IDENTIFIER: US 5955280 A
TITLE: Reverse two-hybrid system

DEPR:

To determine whether the newly isolated alleles exhibit similar phenotypes, protein binding

assays can be used. For example, each E2F allele can be tested in an in vitro binding assay that

involves amplifying, in a PCR reaction, the sequences encoding the various E2F alleles. An

example of an appropriate 5' primer is one which has 25 nucleotides corresponding to the phage T7

RNA polymerase promoter sequence and 20 nucleotides that correspond to the activation domain near

the junction of the activation domain and amino acid 159 of E2F1 (i.e., the first E2F1 amino

acid). A suitable 3' primer is one which corresponds to the 3' end of the E2F1 sequence. The PCR

products from amplification of this sequence can be used in an in vitro transcription/translation

system to generate the corresponding proteins. The mutant proteins can be bound to hybrid

proteins having wild-type DP1 bound to glutathione-S-transferase.

Interacting pairs of proteins

can be purified with glutathione agarose beads, released from the beads, and analyzed by

SDS-polyacrylamide gel electrophoresis.

4. Document ID: US 5885833 A
Entry 4 of 9

File: USPT

Mar 23, 1999

DOCUMENT-IDENTIFIER: US 5885833 A
TITLE: Nucleic acid constructs for the cell cycle-regulated expression of genes and therapeutic methods utilizing such constructs

DEPR:

It has now been found within the scope of the present invention that the B-myb promoter comprises

a high-affinity E2F protein binding site and that the binding of E2F protein

Set Items Description

? s e2f

S1 3400 E2F

? s (dhf or polymerase or pol or myc or myb)(w)promoter??

773 DHF
387509 POLYMERASE
13455 POL
33785 MYC
5559 MYB
224771 PROMOTER??

S2 2360 (DHF OR POLYMERASE OR POL OR MYC OR MYB)(W)PROMOTER??

? s s1 and s2

3400 S1
2360 S2

S3 132 S1 AND S2

? s s3 and py<=1996

Processing

Processing

132 S3

26697399 PY<=1996

S4 89 S3 AND PY<=1996

? rd

...examined 50 records (50)

...completed examining records

S5 34 RD (unique items)

? t s5/3,ab/1-34

5/3,AB/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2000 BIOSIS. All rts. reserv.

10627637 BIOSIS NO.: 199699248782

P120-v-Abl expression overcomes TGF-beta-1 negative regulation of c-myc transcription but not cell growth.

AUTHOR: Birchenall-Roberts Maria C(a); Kim Seong-Jin; Bertolletti Daniel C

Ii; Turley Jennifer M; Fu Tao; Bang Ok-Sun; Kasper James J; Yoo Young Do;

Ruscetti Francis W

AUTHOR ADDRESS: (a)Intramural Res. Support Program, SAIC

Frederick**USA

Natl. Cancer Inst.-Frederick Cancer Res. Development Cent., Frederick, MD

21702

JOURNAL: Oncogene 13 (7):p1499-1509 1996

ISSN: 0950-9232

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Transformation of interleukin-3 dependent (IL-3) 32D-123 myeloid

cells by p120-v-Abl produced the factor-independent 32D-abl cell line. In 32D-abl cells, myc expression was found to be significantly higher than in the parental cells and was correlated with increased E2F1 protein expression and DNA binding ability. Surprisingly, in 32D-abl cells, TGF-beta-1, a potent G-1/S inhibitor of 32D-123 and 32D-abl cell growth, increased %%%E2F%% transactivation as shown by increased c-%%myc%%

%%promoter%%-CAT and GAL4-%%E2F%%-1 activity. In addition, TGF-beta-1 was also found to increase %%%E2F%%-1 protein levels but had no effect

on steady-state retinoblastoma (RB) protein levels or phosphorylation state. In the absence of TGF-beta-1, transient expression of RB in v-Abl expressing cells resulted in decreased c-myc transcription, inhibition of GAL4-%%E2F%%-1 driven transactivation and inhibition of cellular proliferation. RB and v-Abl were found to physically associate in vivo and in vitro via v-Abl's ATP binding region. In summary, these studies

established that in myeloid cells: (1) v-Abl binds RB resulting in increased %%%E2F%%-1-driven c-myc transcription, and (2) an alternative

pathway exists for TGF-beta-1-mediated growth inhibition of v-Abl-transformed cells, in which increased rather than decreased %%%E2F%%-mediated c-myc transcription is observed.

5/3,AB/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2000 BIOSIS. All rts. reserv.

10578232 BIOSIS NO.: 199699199377

%%E2F%% binding is required but not sufficient for repression of B-myc transcription in quiescent fibroblasts.

AUTHOR: Bennett Julie D; Farlie Peter G; Watson Roger J(a)

AUTHOR ADDRESS: (a)Ludwig Inst. Cancer Res., Imperial Coll. Sch. Med. at

St. Mary's, Norfolk Place, London W2 1PG**UK

JOURNAL: Oncogene 13 (5):p1073-1082 1996

ISSN: 0950-9232

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: We have previously shown in mouse NIH3T3 fibroblasts that transcription of the B-myc gene, which encodes a transcription factor required for S phase entry, is repressed through a promoter %%%E2F%% site in G-0/early G-1. Transcription repression at this stage of the cell cycle was correlated with binding of a specific p107/%%E2F%% complex to

this site. We report here, however, that transfection of cells with the known components of this complex, p107, %%%E2F%%-4 and DP-1, did not

repress the B-%%myb%% promoter%% in cycling NIH3T3 cells, although

p107 inhibited transcription transactivation by E2F/DP-1. To establish definitively the contribution of %%%E2F%% to repression, the effects of further mutations within and surrounding the %%%E2F%% site were examined. It was evident that %%%E2F%% binding and repression were closely correlated, lending greater weight to the contention that %%%E2F%% itself is implicated in this activity. These studies also identified a closely linked site, designated the downstream repression site (DRS), which was not required for %%%E2F%% binding or transactivation but which was necessary for repression. These findings indicated that %%%E2F%%-dependent repression and activation are independently regulated phenomena and suggest that repression involves additional interactions determined by the promoter context.

5/3,AB/3 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2000 BIOSIS. All rts. reserv.

10336466 BIOSIS NO.: 199698791384

B-myb promotes S phase and is a downstream target of the negative regulator p107 in human cells.

AUTHOR: Sala Arturo(a); Casella Ida; Bellon Teresa; Calabretta Bruno;

Watson Roger J; Peschle Cesare

AUTHOR ADDRESS: (a)Thomas Jefferson Univ., Dep. Microbiol. Immunol.,

Jefferson Cancer Inst., 233 S. 10th St., Phila**USA

JOURNAL: Journal of Biological Chemistry 271 (16):p9363-9367 1996

ISSN: 0021-9258

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The retinoblastoma protein family has been implicated in growth

control and modulation of the activity of genes involved in cell proliferation, such as B-myb. Recent evidence indicates that the product of the B-myb gene is necessary for the growth and survival of several human and murine cell lines. Upon overexpression, B-myb induces deregulated cell growth of certain cell lines. Here we show that B-myb overexpression is able to induce DNA synthesis in p107 growth-arrested human osteosarcoma cells (SAOS2). p107 might exert its growth-suppressive

09/269321

444 9